

Patent claims

1. Process for preparing (S)-pantoprazole in enantiomerically pure or enantiomerically enriched form by oxidation of 5-difluoromethoxy-2-[(3,4-dimethoxy-2-pyridinyl)methylthio]-1H-benzimidazole, characterized in that the oxidation is carried out in the presence of a chiral zirconium complex or a chiral hafnium complex.
2. Process for preparing (S)-pantoprazole in enantiomerically pure or enantiomerically enriched form by oxidation of 5-difluoromethoxy-2-[(3,4-dimethoxy-2-pyridinyl)methylthio]-1H-benzimidazole, characterized in that the oxidation is carried out in the presence of a chiral zirconium complex.
3. Process according to Claim 1, characterized in that (S)-pantoprazole is obtained in an optical purity of > 90%.
4. Process according to Claim 1, characterized in that the oxidation is carried out using cumene hydroperoxide.
5. Process according to Claim 1, characterized in that zirconium(IV) acetylacetone, zirconium(IV) butoxide, zirconium(IV) tert-butoxide, zirconium(IV) ethoxide, zirconium(IV) n-propoxide, zirconium(IV) isopropoxide or zirconium(IV) isopropoxide/isopropanol complex or hafnium(IV) acetylacetone, hafnium(IV) butoxide, hafnium(IV) tert-butoxide, hafnium(IV) ethoxide, hafnium(IV) n-propoxide, hafnium(IV) isopropoxide or hafnium(IV) isopropoxide/isopropanol complex is used.
6. Process according to Claim 2, characterized in that zirconium(IV) acetylacetone, zirconium(IV) butoxide, zirconium(IV) tert-butoxide, zirconium(IV) ethoxide, zirconium(IV) n-propoxide, zirconium(IV) isopropoxide or zirconium(IV) isopropoxide/isopropanol complex is used.
7. Process according to Claim 1, characterized in that the chiral auxiliary used is a (+)-L-tartaric acid derivative.
8. Process according to Claim 1, characterized in that the chiral auxiliary used is (+)-L-tartaric acid bis-(N,N-diallylamine), (+)-L-tartaric acid bis-(N,N-dibenzylamide), (+)-L-tartaric acid bis-(N,N-diisopropylamide), (+)-L-tartaric acid bis-(N,N-dimethylamide), (+)-L-tartaric acid bis-(N-pyrrolidinamide), (+)-L-tartaric acid bis-(N-piperidinamide), (+)-L-tartaric acid bis-(N-morpholinamide), (+)-L-tartaric acid bis-(N-cycloheptylamine), (+)-L-tartaric acid bis-(N-4-methyl-N-piperazinamide), dibutyl (+)-L-tartrate, di-tert-butyl (+)-L-tartrate, diisopropyl (+)-L-tartrate, dimethyl (+)-L-tartrate or diethyl (+)-L-tartrate.
9. Process according to Claim 1, characterized in that the chiral auxiliary used is (+)-L-tartaric acid bis-(N,N-dimethylamide), (+)-L-tartaric acid bis-(N-pyrrolidinamide) or (+)-L-tartaric acid bis-(N-morpholinamide).

10. Process according to Claim 1, characterized in that the oxidation is carried out in the presence of an organic base.
11. Process according to Claim 1, characterized in that the oxidation is carried out in the presence of a tertiary amine.
12. Process according to Claim 1, characterized in that the oxidation is carried out in organic solvents.
13. Process according to Claim 1, characterized in that the oxidation is carried out in organic solvents comprising 0 to 0.3% by volume of water.
14. Process according to Claim 1, characterized in that the oxidation is carried out in solvents of commercially available quality.
15. Process according to Claim 1, characterized in that the oxidation is carried out in an organic solvent which essentially comprises methyl isobutyl ketone.
16. Process according to Claim 1, characterized in that the zirconium component used is zirconium(IV) acetylacetone, zirconium(IV) butoxide, zirconium(IV) tert-butoxide, zirconium(IV) ethoxide, zirconium(IV) n-propoxide, zirconium(IV) isopropoxide, or zirconium(IV) isopropoxide/isopropanol complex, that the chiral auxiliary used is (+)-L-tartaric acid bis-(N,N-diallylamine), (+)-L-tartaric acid bis-(N,N-dibenzylamine), (+)-L-tartaric acid bis-(N,N-diisopropylamide), (+)-L-tartaric acid bis-(N,N-dimethylamide), (+)-L-tartaric acid bis-(N-pyrrolidinamide), (+)-L-tartaric acid bis-(N-piperidinamide), (+)-L-tartaric acid bis-(N-morpholinamide), (+)-L-tartaric acid bis-(N-cycloheptylamine), (+)-L-tartaric acid bis-(N-4-methyl-N-piperazinamide), dibutyl (+)-L-tartrate, di-tert-butyl (+)-L-tartrate, diisopropyl (+)-L-tartrate, dimethyl (+)-L-tartrate or diethyl (+)-L-tartrate.
17. Process according to Claim 1, characterized in that the zirconium component used is zirconium(IV) acetylacetone, zirconium(IV) butoxide, zirconium(IV) tert-butoxide, zirconium(IV) ethoxide, zirconium(IV) n-propoxide, zirconium(IV) isopropoxide, or zirconium(IV) isopropoxide/isopropanol complex, that the chiral auxiliary used is (+)-L-tartaric acid bis-(N,N-diallylamine), (+)-L-tartaric acid bis-(N,N-dibenzylamine), (+)-L-tartaric acid bis-(N,N-diisopropylamide), (+)-L-tartaric acid bis-(N,N-dimethylamide), (+)-L-tartaric acid bis-(N-pyrrolidinamide), (+)-L-tartaric acid bis-(N-piperidinamide), (+)-L-tartaric acid bis-(N-morpholinamide), (+)-L-tartaric acid bis-(N-cycloheptylamine), (+)-L-tartaric acid bis-(N-4-methyl-N-piperazinamide), dibutyl (+)-L-tartrate, di-tert-butyl (+)-L-tartrate, diisopropyl (+)-L-tartrate, dimethyl (+)-L-tartrate or diethyl (+)-L-tartrate, and that the oxidation is carried out in the presence of an organic base.
18. Process according to Claim 1, characterized in that the zirconium component used is zirconium(IV) n-propoxide, zirconium(IV) isopropoxide or zirconium(IV) isopropoxide/isopropanol complex, that the

chiral auxiliary used is (+)-L-tartaric acid bis-(N,N-dimethylamide), (+)-L-tartaric acid bis-(N-pyrrolidinamide) or (+)-L-tartaric acid bis-(N-morpholinamide) and that the oxidation is carried out using cumene hydroperoxide.

19. Process according to Claim 1, characterized in that the zirconium component used is zirconium(IV) n-propoxide, zirconium(IV) isopropoxide or zirconium(IV) isopropoxide/isopropanol complex, that the chiral auxiliary used is (+)-L-tartaric acid bis-(N,N-dimethylamide), (+)-L-tartaric acid bis-(N-pyrrolidinamide) or (+)-L-tartaric acid bis-(N-morpholinamide) and that the oxidation is carried out using cumene hydroperoxide in the presence of a tertiary amine.

20. (S)-pantoprazole prepared by the process according to Claim 1.